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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,861	04/25/2001	Daniel Dupret	58763.000013	4902

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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/840,861	DUPRET ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,50-80 and 82-95* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,50-80,82-87 and 92-95* is/are rejected.

7)☒ Claim(s) *88-91* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to the Amendment received on December 20, 2004.

Preliminary Remark

The Office acknowledges the submission of claims 93-95 in the Amendment received on December 20, 2004.

Priority

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Rejections - 35 USC § 112

The rejection of claim 69 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, made in Office Action mailed on August 20, 2004 is withdrawn in view of the Amendment received on December 20, 2004.

Claim Rejections - 35 USC § 102

The rejection of claims 1, 50-69, 70-73, 79, 80, 82, 83, 85-87, and 92 under 35 U.S.C. 102(e) as being anticipated by Pachuk et al. (U.S. Patent No. 6,143,527, issued November 7, 2000, filed May 6, 1997, priority May 6, 1996), made in the Office Action mailed on August 20, 2004 is withdrawn in view of the Amendment received on December 20, 2004, amending the claim to become drawn to a method involving the generation of random recombinant polynucleotides as set forth in page 9 of the Applicants' Response.

The rejection of claims 1 and 88-91 under 35 U.S.C. 102(a) as being anticipated by Coco et al. (Nature Biotechnology, April 2001, vol. 19, pages 354-359), made in the Office Action mailed on August 20, 2004 is withdrawn in view of the arguments presented in the Amendment received on December 20, 2004.

Necessitated by Amendment

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 94 is rejected under 35 U.S.C. 102(e) as being anticipated by Pachuk et al. (U.S. Patent No. 6,143,527, issued November 7, 2000, filed May 6, 1997, priority May 6, 1996).

Pachuk et al. disclose an *in vitro* method employing a thermostable ligase, said method comprising the steps of:

i) providing oligonucleotide fragments comprising two heterologous polynucleotide sequences;

ii) hybridizing the fragments to a "bridging" oligonucleotide (or assembly matrix), said fragments oriented for ligation; and

iii) ligating the hybridized fragments having immediately adjacent ends with a ligase to form a recombinant polynucleotide sequence.

While Pachuk et al. recite an additional step of: iv) selecting the recomobinant polynucleotide sequence that exhibits advantageous characteristics compared to corresponding characteristics of one or more reference sequence (Figures 1A, 10A and 10B, columns 3, lines 23-38), the instant claim 94 is drawn to a method which "comprises" the recited steps, allowing the inclusion of additional elements. Further, the method of the instant invention, is in an embodiment, drawn to a method which results in nucleic acids which exhibit biological advantageous characteristics (page 1, 1st paragraph, Specification).

The term, "heterologous," is defined in the instant specification as, "two sequences whose base composition differs by at least one base." [0073]. As the method of Pachuk et al. employs two nucleic acids of at least a single different base, rendering this limitation anticipated.

Figure 1A evidences at least one repetition of providing, hybridizing or the ligating step.

Therefore, Pachuk et al. anticipate the invention as claimed.

With regard to Applicants' argument drawn to the method of Pachuk et al. not being drawn to producing "random recombinant polynucleotide sequences" (page 9, 4th paragraph, Response), the instant claim is not limited to a method producing random recombinant polynucleotides.

Therefore, Pachuk et al anticipate the invention as claimed.

oligonucleotides would occur via use of a ligase (therefore, oriented for ligation) (column 23, lines 24-26).

The recombination procedure would produce a random polynucleotide sequence which would be used again in the same method to produce more recombined polynucleotide sequence (column 23, lines 13-15; column 2, lines 47-50), anticipating claims 1, 50-52, 54, 55, 58, 59-65, 67, 69-72, 74, 79, 82, 86, 87, and 92-95,

With regard to claim 53, Crameri et al., in an embodiment, disclose that a polymerase is employed to fill the gap between the hybridized oligonucleotides (column 23, line 26), followed by the ligation with a ligase (column 23, line 27).

With regard to claim 56, the oligonucleotide are disclosed as being fragmented (column 2, line 56; column 3, lines 1-2).

With regard to claims 57 and 75-78, the artisans disclose that DNAse I is employed to generate random fragments of oligonucleotides (column 7, lines 17-25; column 2, lines 29-30).

With regard to claims 66, 83, and 84, Crameri et al. recite that at least one double stranded assembly (including reassembled nucleic acid) be denatured (claim 14).

With regard to claim 68, Crameri et al. disclose that a thermostable ligase be used (column 23, line 30).

With regard claim 73, Crameri et al. disclose that the reassembled nucleic acid sequence is cloned (column 11, lines 64-65).

With regard to claim 85, Crameri et al. disclose a method of amplifying the reassembled nucleic acids prior to selection (column 12, lines 25-28).

Therefore, Crameri et al. would clearly anticipate the invention as claimed.

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The recombination procedure would produce a random polynucleotide sequence which would be used again in the same method to produce more recombined polynucleotide sequence (column 23, lines 13-15; column 2, lines 47-50), anticipating claims 1, 50-52, 54, 58, 59-65, 67, 69-72, 74, 79, 82, 86, 87, and 92-95,

With regard to claim 53, Crameri et al., in an embodiment, disclose that a polymerase is employed to fill the gap between the hybridized oligonucleotides (column 23, line 26), followed by the ligation with a ligase (column 23, line 27).

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With regard claim 73, Crameri et al. disclose that the reassembled nucleic acid sequence is cloned (column 11, lines 64-65).

With regard to claim 85, Crameri et al. disclose a method of amplifying the reassembled nucleic acids prior to selection (column 12, lines 25-28).

Therefore, Crameri et al. would clearly anticipate the invention as claimed.

Claim Rejections - 35 USC § 103

The rejection of claims 74-78 under 35 U.S.C. 103(a) as being unpatentable over Pachuk et al. (U.S. Patent No. 6,143,527, issued November 7, 2000, filed May 6, 1997, priority May 6, 1996) in view of Stemmer et al. (U.S. Patent No. 6,117,679, issued November 12, 2000, filed March 25, 1996, priority February 17, 1994), made in the Office Action mailed on August 20, 2004 is withdrawn in view of the Amendment received on December 20, 2004, amending the claim to become drawn to a method involving the generation of random recombinant polynucleotides as set forth in page 9 of the Applicants' Response.

The rejection of claims 84 under 35 U.S.C. 103(a) as being unpatentable over Pachuk et al. (U.S. Patent No. 6,143,527, issued November 7, 2000, filed May 6, 1997, priority May 6, 1996) in view of Dolganov (U.S. Patent No. 5,821,091, issued October 13, 1998, filed January 26, 1996), made in the Office Action mailed on August 20, 2004 is withdrawn in view of the Amendment received on December 20, 2004, amending the claim to become drawn to a method involving the generation of random recombinant polynucleotides as set forth in page 9 of the Applicants' Response.

The rejection of claims 88-91 under 35 U.S.C. 103(a) as being unpatentable over Pachuk et al. (U.S. Patent No. 6,143,527, issued November 7, 2000, filed May 6, 1997, priority May 6, 1996) in view of Coco et al. (Nature Biotechnology, April 2001, vol. 19, pages 354-359), made in the Office Action mailed on August 20, 2004 is withdrawn in view of the arguments presented in the Amendment received on December 20, 2004.

Necessitated by Amendment

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 80 is rejected under 35 U.S.C. 103(a) as being unpatentable over Crameri et al. (U.S. Patent No. 6,376,246 B1, issued April 23, 2002, filed September 28, 1999, priority February 5, 1999) in view of Stemmer et al. (U.S. Patent No. 5,830,721, issued November 3, 1998, 102(e) date March 4, 1996).

The teachings of Crameri et al. have already been discussed above.

Crameri et al. do not explicitly teach that a double-stranded heterologous polynucleotides be first denatured prior to the reassembly.

Stemmer et al. teach addition of double-stranded oligonucleotides for generating randomly recombined polynucleotides, wherein said double-stranded oligonucleotides are first denatured prior to their recombination (column 5, lines 54-55).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Stemmer et al. with that of Crameri et al. to arrive at the claimed invention for the following reasons.

It is clear, that when reading the disclosure of Crameri et al., in order for the method of recombination to work, the two oligonucleotides must hybridize to an assembly polynucleotide. Such would necessarily require that the oligonucleotides be single-stranded. Hence, one of ordinary skill in the art at the time the invention was made would have been motivated to first denature the oligonucleotides (if double-

stranded) prior to conducting their hybridization with the assembly matrix polynucleotide. While Cramer et al. are not explicit in disclosing that double-stranded polynucleotides be employed as their initial oligonucleotides, one of ordinary skill in the art would have been motivated to employ any bank of polynucleotides for allowing higher degree of recombination as provided for by Stemmer et al. with a reasonable expectation of success.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Claims 88-91 are objected to for being dependent on a rejected base claim.

The prior art neither teaches or motivates a ligase-mediated recombination method of the instant claims coupled with the use of a degrading enzyme which degrades nonhybridzed ends of the nucleic acid fragments being recombined, wherein said nonhybridized ends overlap hybridized fragments on an assembly matrix.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m. The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Primary Examiner in charge of the prosecution, Dr. Kenneth Horlick, can be reached at (571) 272-0784. If the attempts to reach the above Examiners are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to

the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Young J. Kim
Patent Examiner
Art Unit 1637
4/13/05

YOUNG J. KIM
PATENT EXAMINER

yjk

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

4/18/05